# Clusters of malaria cases at sub-district level in endemic area in Java Island, Indonesia

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# Clusters of malaria cases at sub-district level in endemic area in Java Island, Indonesia

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## Abstract

Malaria remains one of the essential public health problems in Indonesia. The year 2015 was originally set as the elimination target in Java Island, but there are still several regencies on Java reporting malaria cases. Spatial technology helps determine local variations in malaria transmission, control risk areas and assess the outcome of interventions. Information on distribution patterns of malaria at the sub-district level, presented as spatial, temporal, and spatiotemporal data, is vital in planning control interventions. Information on malaria transmission at the sub-district level in three regencies in Java (Banyumas, Kebumen, and Purbalingga) was collected from the Agency for Regional Development (Bappeda), the Population and Civil Registration Agency (Disdukcapil) and Statistics Indonesia (BPS). Global spatial autocorrelation and space-time clustering was investigated together with purely spatial and purely temporal analyses using geographical information systems (GIS) by ArcGis 10.2 and SaTScan 8.0 to detect areas at high risk of malaria. Our results show that malaria was spatially clustered in the study area in central Java, in particular in the Banyumas and Purbalingga regencies. The temporal analysis revealed that malaria clusters predominantly appeared in the period January-April. The results of the spatiotemporal analysis showed that there was one most likely malaria cluster and three secondary clusters in southern central Java. The most likely cluster was located in Purbalingga Regency covering one sub-district and remaining from the beginning of 2016 to the end of 2018. The approach used can assist the setting of resource priorities to control and eliminate malaria.

Key words: Malaria; spatial; temporal; space-time; cluster; sub-district; Indonesia.

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## Introduction

It is estimated that 3.4 billion people in the world are at risk of malaria. The latest factsheet issued by the World Health Organization (WHO) estimates that there were 241 million malaria cases worldwide in 2020, most of whom in Africa where 95% of malaria cases and 96% of malaria deaths occur (WHO, 2022). Several malaria vectors play an essential role in spreading malaria in Java, including *An. maculatus*, *An. balabasensis*, *An. vagus*, *An. aconitus*, *An. kochi*, *An. annularis*, *An. barbirostris* and *An. flavirostris* (Barcus *et al*., 2002; Barodji *et al*., 2003; Siti *et al*., 2020). Mosquito breeding is widespread and includes riverbanks, ponds, springs and rice field basins (Barcus *et al*., 2002). Malaria transmission in Indonesia continues throughout the year but is most pronounced from January to April. Areas with a low endemicity are characterized by an annual parasite incidence (API) <1, moderate APIs vary between 1.0 and 4.9, while highly endemic areas show API values ≥5.0. In 2007, the API was 2.89 per 1000 population, and it is estimated that 45% of the Indonesian population lives in areas at risk of malaria. Out of 495 districts/cities in Indonesia, 396 are malaria-endemic (Roosihermiatie *et al*., 2016).

In 2010, the API rate in Indonesia fell to 1.96 per 1000 population; in 2012 it was still 2.05 but had fallen to 1.32 in 2018 (https://www.statista.com/statistics/705127/number-of-malaria-cases-in-indonesia/). In 2015 an estimated 117,351,457 Indonesians lived in areas at risk of malaria (Murhandarwati *et al.*, 2015). where environmental and behavioural factors influence the spread of malaria. Modelling analysis reveals that rainfall, humidity, temperature and population movement affect the spread of the disease (Rejeki *et al.*, 2018).

There are still malaria cases on the Java Island; the three regencies mentioned reported more than 5500 cases in the period 2009-2019. In Purbalingga Regency from 2010 to 2016, there were still sub-districts in the high case incidence (HCI) category: Pengadegan, Kaligondang, Karangmoncol, Rembang and Purbalingga. In Banyumas Regency, malaria dominated in the sub-districts of south-eastern region, such as Tambak and Sumpiuh with the most characteristics in the 15-54-year age group (63%), the proportion of males were 826 (62%), and the remaining females were 509 (38%) (Dhaniasri *et al.*, 2020). In Kebumen District, the sub-district with the most frequently reported malaria cases were found in Rowokele, Karanggayam and Ayah (Murhandarwati *et al.*, 2015). Most malaria cases occurred in 2009-2012 and tended towards elimination in 2018 (only 12 cases reported). Most malaria cases occurred in Bonorowo sub-district (Health Office Kebumen, 2018).

The results of spatial information are used as a tool in policy formulation, decision-making and/or implementation of activities relating to the control of infectious diseases (Rejeki *et al.*, 2021). Spatial analysis in epidemiology is useful, especially for evaluating different events according to geographic areas and for identifying disease clusters. The benefits of clustering analysis amount to a geographical surveillance of disease presence and the knowledge whether or not clusters are statistically significant. In this way, it can be determined how a disease is distributed in space and time. Spatial analysis can also predict and identify areas at high risk of malaria (Rejeki *et al.*, 2018) and the technique helps epidemiologists to find spatial patterns, identify disease clusters and predict risk.

The use of spatiotemporal in malaria control can determine intervention targets based on local transmission trends (Haque *et al.*, 2011; Alemu *et al.*, 2014; Dhimal *et al.*, 2014; Gebreslasie, 2015). Researchers in several countries, *e.g.*, Ethiopia, Bangladesh, China, Kenya and Brazil, have shown incidence of malaria as well as both primary and secondary spatial clusters (Ernst *et al.*, 2006; Zhang *et al.*, 2008; Haque *et al.*, 2011; Alemu *et al.*, 2013; Kohara Melchior and Neto, 2016) as well as temporal ones (Xia *et al.*, 2015). In the pre-elimination and elimination phases, interventions should be targeted at whole villages or towns with a higher incidence of malaria and malaria episodes in individuals (Bousema *et al.*, 2012). Several spatiotemporal studies based on village as unit have been conducted (Rejeki *et al.*, 2019), but sub-district analysis is still lacking.

The problems related to malaria that have currently occurred in Indonesia include low awareness and low community participation in malaria prevention and lack of resources, especially with respect to financing (Ahmad *et al.*, 2021). Various efforts have been made to achieve the elimination target set, including the use of mosquito nets, indoor residual spraying (IRS) and mass testing, but the results are still not optimal (Rejeki *et al.*, 2019). The purpose of this study was to analyse the purely spatial, purely temporal and spatiotemporal incidence of malaria at the sub-district level in Banyumas, Purbalingga, and Kebumen regencies on the island of Java in an effort to create a basis for control plans.

## Materials and methods

### Study area and population

Central Java Province covers 32,801 km$^2$, and the three regencies Banyumas, Purbalingga and Kebumen 3386.6 km$^2$ (Figure 1).

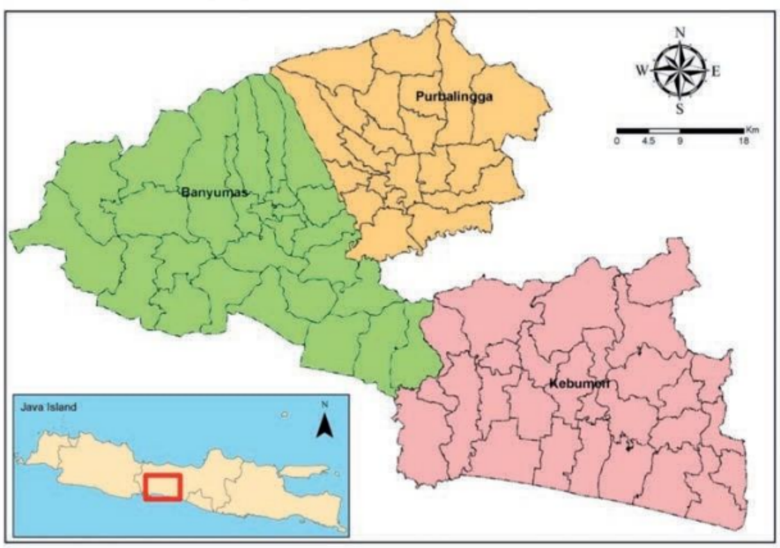


**Figure 1. Study area endemic for malaria including three regencies in central Java.**

These three regencies have a similar topography and general geography. The combined population amounts to 3,799,409 people at the latest census. The endemicity was categorized based on API, which in these three districts is currently less than 1/10,000 of the population (between 0.004 and 0.42 by mile$^2$ or 0.010 and 1.09 km$^2$), *i.e.* the research location is a low malaria-endemic area.

## Data sources

During the last ten years, there were 1624 malaria cases reported in Banyumas, 2029 in Purbalingga, and 1940 in Kebumen. This research used data for the period 2010-2018. It covered the number of malaria cases per month for these nine years based on sub-district centroid coordinates and annual sub-district population. This information was obtained from Statistics Indonesia (BPS), the Agency for Regional Development (Bappeda), the Population and Civil Registration Agency (Disdukcapil) and the Health Offices in the three regencies. The unit of analysis in this study included 75 sub-districts, *i.e.* 27 sub-districts in Banyumas, 22 in Purbalingga and 26 in Kebumen.

## Statistics

The data analysis included global spatial autocorrelation analysis based on Global Moran's *I* (Arselin, 1995), purely spatial analysis to detect risky locations, purely temporal clustering to detect at-risk time periods, space-time clustering to detect malaria clustering based on place and time. The software used in this analysis was ArcGIS 10.2 (ESRI, Redlands, CA, USA) and SaTScan, version 8.0 (Kulldorff, 2015). Temporal analysis was used to detect the classification of malaria by the time of year from 2010-2018 with an aggregation of 1 month. The analysis in this study used four stages: i) spatial autocorrelation analysis; ii) pure spatial cluster analysis; and iii) pure temporal analysis; and iv) spatiotemporal cluster analysis. Spatial autocorrelation analysis was used to determine the distribution pattern in all sub-districts in the research location each year. Determination of the distribution pattern of malaria (cluster, random and dispersion) was based on Z value and the level of significance (P-value). The SaTScan was operated by the application of circular windows of various sizes covering the areas/times under study to detect high-risk clustering of cases. The observed cases were compared with the expected cases inside and outside each window and the risk ratio was estimated based on Poison distribution. In this study, the maximum spatial cluster size of the population was set at 20% and the maximum temporal cluster size was adopted with a default value of 50%.

Spatial autocorrelation analysis by Global Moran's *I* was applied for the determination of the distribution pattern of malaria cases in three regencies every year to get an understanding whether the distribution pattern of malaria in the three districts was clustered, dispersed or random.

# Results

## Global Moran's *I*

Table 1 shows that in principle all annual malaria cases in Banyumas, Purbalingga and Kebumen were clustered. The number of sub-districts that reported malaria cases between 2010 and 2018 ranged from 10 to 26 sub-districts, and a downward trend was evident during the last five years.

## SaTScan

The analysis results showed that the malaria cases from 2010-2018 were not randomly distributed in Java. Kulldorff's spatial scan statistical method assisted in identifying 11 different spatially significant clusters (one most likely cluster and ten likely secondary clusters), with one or two clusters per year. Table 2 shows all malaria clusters detected by purely spatial clustering in the study period.

The data presented in Table 1 are shown in map format in Figure 2. As can be seen in both Table 2 and Figure 2, there was only one primary cluster, which occurred in 2011 covering only one sub-district in Purbalingga Regency. In contrast, the occurrence of first and second secondary clusters varied both temporally and spatially though most of them were limited in size.

## Temporal analysis

The temporal clusters were divided into monthly occurrences (Table 3); the incidence of malaria was clustered in January-February in 2010-2014 and in April in 2016, while there were no significant temporal clustering in 2015, 2017 and 2018. In general, malaria clusters occurred at the beginning of the year, *i.e.* January-April.

## Spatial analysis

Spatial analysis using SaTScan from 2010-2018 showed that only one sub-district was in the most likely cluster category, while

**Table 1. Incidence and results of the Global Moran spatial analysis.**

| Year | N | Case (no.) | *I* | Z | P-value | Pattern |
|---|---|---|---|---|---|---|
| 2010 | 26 | 1582 | 0.74 | 26.18 | 0.000 | Clustered |
| 2011 | 21 | 643 | 0.47 | 12.75 | 0.000 | Clustered |
| 2012 | 23 | 369 | 0.77 | 19.02 | 0.000 | Clustered |
| 2013 | 19 | 232 | 0.64 | 20.98 | 0.000 | Clustered |
| 2014 | 13 | 131 | 0.22 | 4.49 | 0.000 | Clustered |
| 2015 | 10 | 38 | 0.23 | 2.68 | 0.007 | Clustered |
| 2016 | 17 | 187 | 0.54 | 10.36 | 0.000 | Clustered |
| 2017 | 15 | 24 | 0.19 | 2.42 | 0.015 | Clustered |
| 2018 | 14 | 54 | 0.48 | 7.97 | 0.000 | Clustered |

N, the number of sub-districts reporting malaria cases; *I*, Global Moran's coefficient; Z, outcome of the Global Moran examination.

likely secondary clusters ranged from one to five sub-districts (Table 2). This most likely clusters occurred in Purbalingga Regency, and the secondary clusters occurred in three districts (Figure 3). These three districts were in border areas where vector and human migration contributed to malaria transmission. The results showed that the research area still kept the potential for malaria transmission to occur.

### Spatiotemporal analysis

As seen in Table 4, the most likely cluster in January 2016 to December 2018 time interval involved Banyumas and Purbalingga. The first secondary cluster was from May 2012 to December 2015 in Purbalingga, while the second covered sub-districts in Banyumas from August 2011 to January 2012. The third

**Table 2. Malaria clusters detected by purely spatial clustering in 2010-2018.**

| Year | Type | N | Coordinates (radius) | Observed | Expected | RR | LLR | P-value |
|---|---|---|---|---|---|---|---|---|
| 2010 | B1 | 4 | –7263 S; 109,462 E 7.35 km | 803 | 778.21 | 1.06 | 0.776 | 0.98 |
| 2011 | A | 1 | –7287 S; 109,525 E 0 km | 117 | 80.18 | 1.56 | 8.624 | 0.001 |
| 2012 | B1 | 1 | –7531 S; 109,272 E 0 km | 38 | 24.87 | 1.59 | 3.234 | 0.231 |
| | B2 | 2 | –7287 S; 109,525 E 7.35 km | 35 | 26.70 | 1.34 | 1.274 | 0.847 |
| 2013 | B1 | 1 | –7455 S; 109,370 E 0 km | 2 | 1.01 | 1.99 | 0.380 | 0.98 |
| 2014 | B1 | 2 | –7263 S; 109,462 E 4.85 km | 4 | 2.28 | 1.78 | 0.542 | 0.96 |
| | B2 | 1 | –7370 S; 109,435 E 0 km | 40 | 37.23 | 1.11 | 0.141 | 0.98 |
| 2015 | B1 | 5 | –7595 S; 109,367 E 26.14 km | 19 | 17.97 | 1.12 | 0.056 | 1.00 |
| 2016 | B1 | 1 | –7777 S; 109,798 E 0 km | 2 | 1.39 | 1.44 | 0.117 | 1.00 |
| 2017 | B1 | 5 | –7512 S; 109,053 E 34.50 km | 11 | 8.19 | 1.63 | 0.700 | 0.94 |
| 2018 | B1 | 2 | –7785 S; 109,790 E 0 km | 2 | 1.44 | 1.40 | 0.098 | 1.00 |

N, number of sub-district clusters detected; RR, relative risk; LLR, log-likelihood ratio; A, primary cluster; B1, first secondary cluster; B2, second secondary cluster.

**Table 3. Malaria clusters detected by purely temporal clustering in 2010-2018.**

| Year | Cluster time frame | Observed | Expected | RR | LLR | P-value |
|---|---|---|---|---|---|---|
| 2010 | 1/1/2010-31/1/2010 | 150 | 41.77 | 3.86 | 87.43 | 0.001 |
| 2011 | 1/1/2011-31/1/2012 | 132 | 22.52 | 7.12 | 143.25 | 0.001 |
| 2012 | 1/2/2012-29/2/2012 | 100 | 33.69 | 3.70 | 49.60 | 0.001 |
| 2013 | 1/1/2013-31/1/2013 | 26 | 7.96 | 3.55 | 13.48 | 0.001 |
| 2014 | 1/1/2014-31/1/2014 | 14 | 3.65 | 4.17 | 8.90 | 0.002 |
| 2015 | 1/5/2015-30/9/2015 | 19 | 13.76 | 1.76 | 1.50 | 0.59 |
| 2016 | 1/4/2016-30/4/2016 | 58 | 27.35 | 2.62 | 16.09 | 0.001 |
| 2017 | 1/8/2017-30/11/2017 | 8 | 5.21 | 1.80 | 0.86 | 0.85 |
| 2018 | 1/3/2018-31/7/2018 | 35 | 30.47 | 1.42 | 0.79 | 0.93 |

RR, relative risk; LLR, log-likelihood ratio.

**Table 4. Space-time malaria clusters detected in 2010-2018.**

| Cluster type | Time | Coordinates (radius) | Observed | Expected | RR | P-value |
|---|---|---|---|---|---|---|
| A | 1/1/2016-31/12/2018 | –7379 S/109,321 E 9.19 km | 204 | 17.88 | 11.41 | <0.001 |
| B1 | 1/5/2012-31/12/2015 | –7362 S/109,480 E 8.5 km | 370 | 105.16 | 3.52 | <0.001 |
| B2 | 1/8/2011-31/1/2012 | –7600 S/109,409 E 0 km | 170 | 28.97 | 5.87 | <0.001 |
| B3 | 1/1/2010-31/1/2010 | –7287 S/109,525 E 7.35 km | 891 | 516.3 | 1.73 | <0.001 |

RR, relative risk.

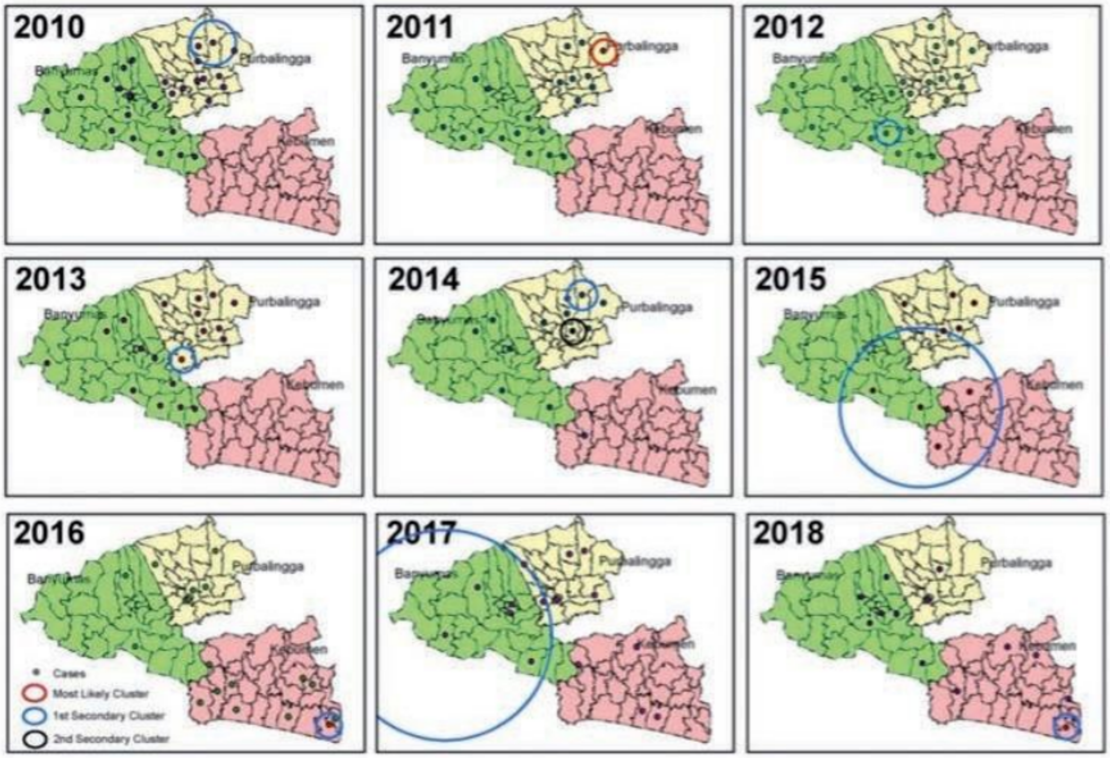


**Figure 2. Annual spatial malaria clusters detected by purely temporal analysis.**

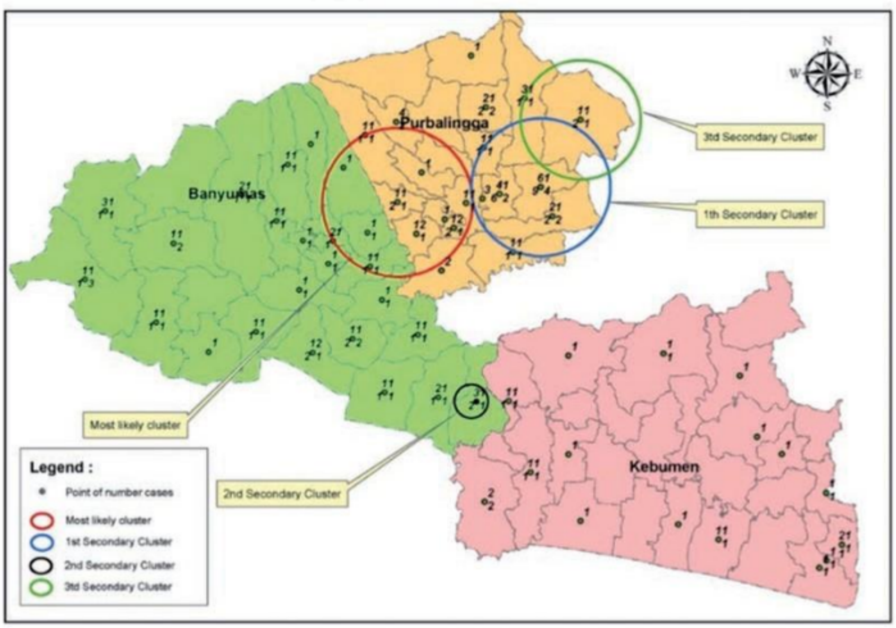

**Figure 3. Space-time malaria clusters detected 2010-2018.**

secondary cluster appeared in Purbalingga from January to December 2010.

## Discussion

The clusters of malaria cases found in some of the sub-districts belonging to the regencies of central Java indicates that local transmission is still ongoing at the study site due to the local presence of vectors, environmental conditions together with human behaviour and lack of uninterrupted prevention. The results of this study are in line with research in Hubei Province, China, that identified 11 districts at high risk of malaria based on purely spatial analysis in 2004-2011 (Xia *et al*., 2015). The results are also supported by previous research in another part of Java (Menoreh), which also showed that malaria cases were clustered in areas across provincial borders (Rejeki, *et al*., 2019).

The division of the search for temporal clusters into monthly occurrences showed that the malaria clustering generally occurred in the beginning of the period January-April. It means that vector control measures must be activated before January. This important finding is supported by previous research on the behaviour of malaria vectors: *An. balabacensis* appears more often in the rainy season (October-April), while the *An. maculatus* population increases in the dry season (Barcus *et al*., 2002). Obviously, transmission is connected with the predominant weather systems that vary between countries, *e.g*., a study in Peru that identified clusters temporally found them occurring from April to July (Rosas-Aguirre *et al*., 2015). A study in China revealed that the cluster presence varies from year to year, namely in 2004-2005 in June-September, in 2007-2010 in May-September and in 2011 in February-June (Xia *et al*., 2015).

Our Spatiotemporal analysis of malaria presence over the nine-year period 2010-2018 identified four clusters. The most likely one was located in Purbalingga Regency, while the secondary clusters were found in various sub-districts of Banyumas and Purbalingga proving that these two regencies are vulnerable areas for malaria transmission. Therefore, malaria control efforts here must be carried out simultaneously in a comprehensive and continuous way. A rapid response from the team across these two regencies is needed to reduce the transmission period. This team is thus expected to be able to move quickly without the obstacle of decentralization that may delay the financing of the interventions needed (Andono *et al*., 2020). Malaria studies on cross-border malaria, such as in China-Laos (Xu and Liu, 2012), China-Vietnam (Xu *et al*., 2017), Mozambique-South Africa/Swaziland (Moonasar *et al*., 2016) are examples of the need for coordination and joint management of the malaria problem between countries.

## Conclusions

This study reveals that malaria is still a significant health problem in Java. It is supported by the finding of malaria clusters based on spatial, temporal and spatiotemporal research. The data presented here can be the basis for joint control planning of malaria interventions in Java, especially in the sub-districts of Banyumas, Purbalingga and Kebumen.

## References

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